64-13

(9)

~~THE~~ QUATERLY ~~(1)~~ REPORT ~~ON~~ No. 1, 2 / 1 - 61-31 Jan 62 (1a)

CONTRACT ~~NO~~ DA 92 / 557 - FEC - 35675

INCLUSIVE ~~DATES~~ ~~October 27, 1961~~ TO ~~January 31, 1962~~

~~SUBJECT OF INVESTIGATION~~

(6)

EXPLORATION OF NEW CHEMOTHERAPEUTICS
FOR
INFECTIOUS DISEASES

(10)

RESPONSIBLE INVESTIGATOR

~~Dr. Toju Hata, M.D.~~
President
Kitasato Institute for Infectious Diseases
~~Head of Antibiotic Division of the said Institute~~

U.S. Army Research & Development Group (9852) (Far East)
Office of the Chief of Research and Development
United States Army
APO 343

EXPLORATION OF NEW CHEMOTHERAPEUTICS FOR INFECTIOUS DISEASES

Fundamental Studies on Protomycin, an Antiamaebic Antibiotic and Cephalomycin, an Antiviral Antibiotic

Toju Hata,
Ryozo Sugawara, Akihiro Matsumae
and
Hiroshi Yamamoto

Kitasato Institute
for
Infectious Diseases
Tokyo, Japan

We continued the studies on the degradation products of protomycin (I), of which physicochemical and biological characters has been described in the final report (2).

The main products may be summerized as follows:

Tetrahydroprotomycin (II), $C_{19}H_{33}NO_5$, was obtained by the catalytic hydrogenation with Pd-Carbon of protomycin (I) in glacial acetic acid.

3,5-dimethyl-3,5-heptadiene-2-one (III) and acetone (IV) were proved as volatile ketones arising from alkaline degradation of protomycin.

3,5-dimethyl-2-heptanone (V) and acetone (VI) were identified by alkaline degradation of tetrahydroprotomycin.

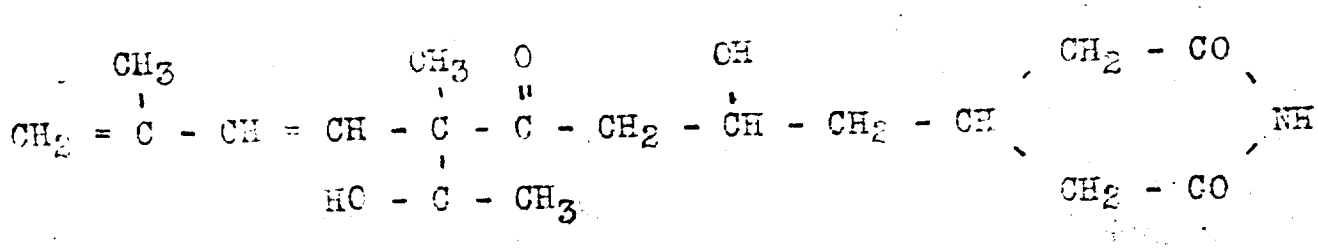
Formaldehyde (VII) and acetaldehyde (VIII) were proven by ozonolysis of protomycin.

Acetone (IX) and methylethylketone (X) were obtained from the residual squeous solution of ozonolysis after alkaline degradation.

The oxime of tetrahydroprotomycin, although it remained oil, were treated with cono. H_2SO_4 to induce Beckmann rearrangement and thereafter steam distiled from acidic solution. An acid with molecular formular of $C_{10}H_{19}COOH$ was obtained as p-phenylazophenacyl ester (XI).

Tetrahydroprotomycin gave the benzylamine reaction product (XII), which was identified with the corresponding one from tetrahydroprotomycin.

These products from (I) through (XII) were found to be explained well by the chemical structure:



Tentative Structure of Protomycin

Cephalomycin, an antiviral antibiotic, was separated into two fractions as described in p. 17 of the final report (2). Each of these fractions gave a single spot when tested on electrophoretic paperchromatography.

The fraction A migrated as alubumin and Fraction B as gamma globulin.

The activity was higher in the former than in the latter.

The result is to be made publish at the Symposium for the Antiviral substance, March 3, 1962.